

STATUS OF THE CLAIMS

1-31. Cancelled

32. (Withdrawn) A method for identifying receptors, comprising:

(a) introducing a first polynucleotide encoding a receptor into a cell, wherein the receptor comprises a ligand binding domain for a target ligand operably linked to a polynucleotide binding domain so that binding of the target ligand to the receptor activates transcription of a second polynucleotide complementing a selection agent; and

(b) culturing the cell on the selective media in the presence of the target ligand, wherein growth of the cell indicates interaction of the receptor with the target ligand.

33. (Withdrawn) The method of claim 32, further comprising culturing the cell on selective media in the absence of the target ligand, wherein growth of the cell indicates the receptor constitutively activates transcription of the second polynucleotide.

34. (Withdrawn) A cell comprising:

(a) a recombinant nuclear receptor that induces expression of a first polynucleotide in response to interaction with a target small molecule, wherein expression of the first polynucleotide complements a selective agent; and

(b) an adapter fusion protein comprising a human coregulator domain operably linked to an activation domain, wherein the adapter fusion protein enhances transcription of the first polynucleotide induced by the recombinant nuclear receptor.

35. (Withdrawn) The cell of claim 34, wherein the cell is a yeast cell.

36. (Withdrawn) The cell of claim 34, wherein the human coregulator domain is a coactivator domain selected from the group consisting of SRC-1 and ACTR.

37. (Withdrawn) A method for identifying enzymes comprising:

(a) introducing a first polynucleotide into a cell that is unable to grow on selective media, wherein the cell expresses a recombinant receptor polypeptide that activates transcription of a second polynucleotide in response to interaction of the recombinant receptor polypeptide with a target substance and wherein the first polynucleotide encodes a polypeptide that produces the target substance;

- (b) culturing the cell on the selective media; and
- (c) selecting the cell that grows on the selective media.

38. (Withdrawn) The method of claim 37, wherein the selective media does not contain an amino acid necessary for survival.

39. (Withdrawn) The method of claim 38, wherein the amino acid is selected from the group consisting of histidine and alanine.

40. (Withdrawn) The method of claim 37, wherein the first polynucleotide encodes an enzyme that produces the target substance.

41. (Withdrawn) The method of claim 37, wherein the first polynucleotide encodes an engineered enzyme.

42. (Withdrawn) The method of claim 37, wherein the first polynucleotide encodes a naturally occurring enzyme.

43. (Withdrawn) The method of claim 37, wherein the transformed cell further expresses an adaptor fusion protein comprising a human coregulator domain operably linked to an activation domain, wherein the adaptor fusion protein enhances transcription of the first polynucleotide induced by the recombinant receptor polypeptide.

44. (Withdrawn) The method of claim 37, wherein the adaptor fusion protein comprises a human coactivator for transcription of the second polynucleotide.

45. (Withdrawn) The method of claim 37, wherein introducing a first polynucleotide into the cell comprises introducing a plurality of polynucleotides encoding enzymes having different substrates into the cell, and wherein growth of a cell on the selective media indicates that the plurality of polynucleotides encode enzymes for producing products that complement the selective media.

46. (Withdrawn) The method of claim 45, wherein the product of one of the enzymes is the substrate of another of the enzymes.

47. (Withdrawn) A method for selecting cells comprising:

- (a) introducing a first polynucleotide into a cell, wherein the cell expresses a recombinant receptor polypeptide that activates transcription of a second polynucleotide in response to interaction of the recombinant receptor polypeptide with a target substance;
- (b) culturing the cell on selective media in the presence of a first selection agent; and
- (c) selecting the cell that survives on the selective media in the presence of the selection agent, wherein expression of the second polynucleotide inhibits growth of the cell.

48-60 (Canceled).

61. (New) A yeast cell comprising:

- a first heterologous polynucleotide, said heterologous polynucleotide encoding a heterologous polypeptide, wherein said heterologous polypeptide has an enzymic activity characterized by generating a candidate nuclear receptor ligand from a substrate; and
- a yeast transcription modulating system comprising a recombinant nuclear receptor polypeptide, wherein the recombinant nuclear receptor polypeptide, when expressed in the yeast cell in the presence of the nuclear receptor ligand binding to the recombinant nuclear receptor polypeptide, activates expression of a genetic locus, and further comprising an adapter polypeptide, wherein the recombinant nuclear receptor polypeptide and the adapter polypeptide are each independently encoded by individual heterologous polynucleotides or are encoded by the same heterologous polynucleotide.

62. (New) The yeast cell according to claim 61, wherein the recombinant nuclear receptor polypeptide comprises a ligand-binding domain operably linked to a DNA-binding domain and optionally to a flexible hinge domain.

63. (New) The yeast cell according to claim 61, wherein the adapter polypeptide comprises a coactivator domain operably linked to a yeast transcriptional activator.

64. (New) The yeast cell according to claim 62, wherein the ligand-binding domain of the recombinant nuclear receptor polypeptide is derived from a ligand-binding domain of a human nuclear receptor polypeptide, or a variant thereof.

65. (New) The yeast cell according to claim 63, wherein the coactivator domain of the adapter polypeptide is derived from a coactivator domain of a human coactivator, or a variant thereof, and wherein the coactivator cooperatively binds to the ligand-binding domain of the recombinant nuclear receptor polypeptide in the presence of a ligand to activate expression of a genetic locus.

66. (New) The yeast cell according to claim 61, wherein expression of the genetic locus allows proliferation of the yeast cell on a selective medium.

67. (New) The yeast cell according to claim 61, wherein expression of the genetic locus inhibits proliferation of the yeast cell on a selective medium.

68. (New) The yeast cell according to claim 68, wherein the selective medium comprises 5-fluoroorotic acid.

69. (New) The yeast cell according to claim 69, wherein the expressed genetic locus encodes orotidine-5'-phosphate decarboxylase.

70. (New) The yeast cell according to claim 70, wherein the first heterologous polynucleotide encodes a modified enzyme, wherein said modified enzyme catalyzes a receptor ligand characterized as binding to the recombinant receptor polypeptide.